

What is claimed is:

1. An isolated and purified superantigen toxin DNA fragment which has been altered such that  
5 binding of the encoded altered toxin to either the MHC class II or T cell antigen receptor is altered.
2. An isolated and purified DNA fragment according to claim 1, wherein said superantigen toxin  
10 is toxic shock syndrome toxin-1 having the sequence of SEQ ID NO:11 or a portion thereof, or an allelic portion thereof
3. An isolated and purified DNA fragment  
15 according to claim 1, wherein said superantigen toxin is Staphylococcal enterotoxin C1 having the sequence of SEQ ID NO:13 or a portion thereof, or an allelic portion thereof.
- 20 4. An isolated and purified DNA fragment according to claim 1, wherein said superantigen toxin is Streptococcal pyrogenic exotoxin A having the sequence of SEQ ID NO:15 or a portion thereof, or an allelic portion thereof.
- 25 5. An isolated and purified DNA fragment according to claim 1, wherein said superantigen toxin is toxic shock syndrome toxin-1 having the sequence of SEQ ID NO:11 or a portion thereof, or an allelic  
30 portion thereof further comprising a mutation wherein said mutation results in a change in histidine 135 of said toxin from histidine to alanine.
6. An isolated and purified DNA fragment  
35 according to claim 1, wherein said superantigen is

Streptococcal pyrogenic exotoxin A fused to Streptococcal pyrogenic exotoxin B, wherein said DNA has the sequence of SEQ ID NO:23.

- 5                   7. An isolated and purified DNA fragment according to claim 2, wherein said fragment encodes the amino acid sequence of SEQ ID NO:12 or a portion thereof, or an allelic portion thereof.
- 10                   8. An isolated and purified DNA fragment according to claim 3, wherein said fragment encodes the amino acid sequence of SEQ ID NO:14 or a portion thereof, or an allelic portion thereof.
- 15                   9. An isolated and purified DNA fragment according to claim 4, wherein said fragment encodes the amino acid sequence of SEQ ID NO:16 or a portion thereof, or an allelic portion thereof.
- 20                   10. An isolated and purified DNA fragment according to claim 6, wherein said fragment encodes the amino acid sequence of SEQ ID NO:27 or a portion thereof, or an allelic portion thereof.
- 25                   11. A recombinant DNA construct comprising:  
                    (i) a vector, and  
                    (ii) an isolated and purified altered superantigen toxin DNA fragment according to claim 1.
- 30                   12. A recombinant DNA construct according to claim 11, wherein said DNA fragment has the sequence according to SEQ ID NO:11 or a portion thereof, or an allelic portion thereof.

13. A recombinant DNA construct according to claim 11, wherein said DNA fragment has the sequence according to SEQ ID NO:13 or a portion thereof, or an allelic portion thereof.

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14. A recombinant DNA construct according to claim 11, wherein said DNA fragment has the sequence according to SEQ ID NO:15 or a portion thereof, or an allelic portion thereof.

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15. A recombinant DNA construct according to claim 11, wherein said DNA fragment has the sequence according to SEQ ID NO:23 or a portion thereof, or an allelic portion thereof.

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16. The recombinant DNA construct according to claim 12, wherein said DNA fragment encodes the amino acid sequence specified in SEQ ID NO:12.

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17. The recombinant DNA construct according to claim 13, wherein said DNA fragment encodes the amino acid sequence specified in SEQ ID NO:14.

18. The recombinant DNA construct according to claim 14, wherein said DNA fragment encodes the amino acid sequence specified in SEQ ID NO:16.

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19. The recombinant DNA construct according to claim 15, wherein said DNA fragment encodes the amino acid sequence specified in SEQ ID NO:27.

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20. A recombinant DNA construct according to claim 16 wherein said construct is pETTST30.

21. A recombinant DNA construct according to claim 17 wherein said construct is pETSEC45.

22. A recombinant DNA construct according to  
5 claim 18 wherein said construct is pETSPEA42.

23. A recombinant DNA construct according to claim 11, wherein said vector is an expression vector.

10 24. A host cell transformed with a recombinant DNA construct according to claim 11.

25. A host cell transformed with a recombinant construct according to claim 20.

15 26. A host cell transformed with a recombinant construct according to claim 21.

20 27. A host cell transformed with a recombinant construct according to claim 22.

28. A method for producing altered superantigen toxin comprising culturing the cells according to claim 24, under conditions such that said  
25 DNA fragment is expressed and said superantigen toxin is thereby produced, and isolating said superantigen toxin.

29. A method for producing altered  
30 superantigen toxin comprising culturing the cells according to claim 25, under conditions such that said DNA fragment is expressed and said superantigen toxin is thereby produced, and isolating said superantigen toxin.

30. A method for producing altered  
superantigen toxin comprising culturing the cells  
according to claim 26, under conditions such that said  
5 DNA fragment is expressed and said superantigen toxin  
is thereby produced, and isolating said superantigen  
toxin.

31. A method for producing altered  
10 superantigen toxin comprising culturing the cells  
according to claim 27, under conditions such that said  
DNA fragment is expressed and said superantigen toxin  
is thereby produced, and isolating said superantigen  
toxin.

32. An isolated and purified superantigen  
toxin which has been altered such that binding of the  
encoded altered toxin to either the MHC class II or T  
cell antigen receptor is altered.

20 33. An isolated and purified superantigen  
toxin according to claim 32 wherein said toxin is  
staphylococcal toxin shock syndrome toxin-1.

25 34. An isolated and purified superantigen  
toxin according to claim 32 wherein said toxin is  
staphylococcal enterotoxin C1.

30 35. An isolated and purified superantigen  
toxin according to claim 32 wherein said toxin is  
streptococcal pyrogenic exotoxin A.

35 36. An isolated and purified superantigen  
toxin according to claim 32 wherein said toxin is  
TSST-1.

37. An altered TSST-1 superantigen toxin peptide according to claim 36 wherein position 30 has been changed to alanine or arginine.

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38. An altered TSST-1 superantigen toxin peptide according to claim 36 wherein position 135 has been changed to alanine.

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39. An altered TSST-1 superantigen toxin peptide according to claim 36 wherein position 30 has been altered to arginine and position 135 has been altered to alanine.

15

40. An altered SEC1 superantigen toxin peptide according to claim 34 wherein position 45 has been altered to lysine.

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41. An altered SpeA superantigen toxin peptide according to claim 35 wherein position 42 has been altered to alanine or arginine.

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42. An altered SpeA superantigen toxin according to claim 41 fused to an altered SpeB superantigen toxin peptide wherein said SpeB peptide position 47 has been altered to serine.

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43. The altered superantigen of claim 42 having amino acid SEQ ID NO:27.

44. A method for the diagnosis of superantigen-associated bacterial infection comprising the steps of:

(i) contacting a sample from an individual suspected of having a superantigen-associated

bacterial infection with altered superantigen toxin;  
and

- (ii) detecting the presence or absence of a  
superantigen-associated bacterial infection by  
5 detecting the presence or absence of a complex formed  
between the altered superantigen toxin and antibodies  
specific therefor in the sample.

45. A method for the diagnosis of a  
10 superantigen toxin-associated bacterial infection  
according to claim 40 wherein the altered superantigen  
toxin is chosen from the group consisting of SpeA,  
SEB, SEA, TSST-1, SEC-1.

15 46. A superantigen toxin-associated  
infection diagnostic kit comprising an altered  
superantigen toxin according to claim 32 wherein said  
toxin is chosen from the group consisting of SpeA,  
SEB, SEA, TSST-1, and SEC-1, and ancillary reagents  
20 suitable for use in detecting the presence or absence  
of antibodies against superantigen toxin in a  
mammalian sample.

47. A vaccine comprising an altered  
25 superantigen toxin according to claim 32 effective for  
the production of antigenic and immunogenic response  
resulting in the protection of a mammal against  
superantigen-associated bacterial infection.

30 48. A vaccine according to claim 47 wherein  
said altered superantigen toxin is chosen from the  
group consisting of SpeA, SEB, SEA, TSST-1, and SEC-1.

49. A vaccine according to claim 48 wherein said SpeA toxin further comprises an altered SpeB superantigen peptide.

5 50. A vaccine according to claim 48 wherein said vaccine further comprises at least one other different altered superantigen toxin chosen from the group consisting of SpeA, SEB, SEA, TSST-1, and SEC-1.

10 51. A multivalent vaccine against superantigen-associated bacterial infections comprising a combination of altered superantigen toxins selected from the group consisting essentially of TSST-1, SpeA , SEA, SEB, SEC-1, or any portion or  
15 allelic form thereof, capable of eliciting protective antibodies against superantigen toxins in a pharmaceutically acceptable excipient in a pharmaceutically acceptable amount.

20 52. A multivalent vaccine according to claim 51 further comprising an altered SpeA superantigen or peptide thereof fused to an altered SpeB superantigen or peptide thereof.

25 53. A therapeutic method for the treatment or amelioration of a superantigen-associated bacterial infection said method comprising administering to an individual in need of such treatment an effective amount of sera from individuals immunized with one of  
30 more altered superantigen toxin vaccine according to claim 47 in a pharmaceutically acceptable dose in a pharmaceutically acceptable excipient.

35 54. A therapeutic method for the treatment or amelioration of a superantigen-associated bacterial

infection, said method comprising administering to an individual in need of such treatment an effective amount of antibodies against altered superantigen toxins in a pharmaceutically acceptable dose in a  
5 pharmaceutically acceptable excipient.

55. A therapeutic method for the treatment or amelioration of a superantigen-associated bacterial infection, said method comprising administering to an  
10 individual in need of such treatment an effective amount of altered superantigen toxins from streptococcal and staphylococcal bacteria in order to inhibit adhesion of superantigen bacterial toxin to MHC class II or T cell receptors by competitive inhibition  
15 of these interactions in a pharmaceutically acceptable dose in a pharmaceutically acceptable excipient.

56. A therapeutic method for the treatment of diseases that may not be associated directly with  
20 superantigen toxins by causing specific nonresponsiveness of T cell subsets or by expanding or stimulating specific T cell subsets, in vivo or ex vivo by use of altered superantigen toxin.

25 57. Antisera isolated from individuals immunized with one or more altered TSST-1 superantigen toxin.

58. Antisera according to claim 57 wherein  
30 said altered superantigen toxin TSST-1 comprises TSST-1 wherein position 30 has been altered to arginine or alanine.

59. Antisera according to claim 57 wherein  
35 said altered superantigen toxin TSST-1 comprises TSST-

1 wherein position 30 has been altered to arginine or  
alanine and position 135 has been altered to alanine.

60. Antisera according to claim 57 wherein  
5 said altered superantigen toxin is SEC1.

61. Antisera according to claim 60 wherein  
said SEC1 position 45 has been altered to lysine.

10 62. Antisera according to claim 57 wherein  
said altered superantigen toxin is SpeA.

63. Antisera according to claim 62 wherein  
said SpeA position 42 has been altered to alanine.

15 64. Antisera according to claim 62 wherein  
said SpeA position 42 has been altered to arginine.

65. Antisera according to claim 57 wherein  
20 said altered superantigen toxin is SpeA wherein said  
SpeA position 42 has been altered to alanine, and said  
SpeA fused to an altered SpeB superantigen toxin  
wherein said SpeB position 47 has been altered to  
serine.

25 66. An antibody which recognizes altered  
TSST-1.

67. An antibody according to claim 66  
30 wherein said TSST-1 comprises a change to arginine at  
position 30.

68. An antibody according to claim 66  
wherein said TSST-1 comprises a change to alanine at  
35 position 30.

69. An antibody which recognizes altered  
SEC1.

5               70. An antibody according to claim 69  
wherein said SEC-1 comprises a change to lysine at  
position 45.

10              71. An antibody which recognizes altered  
SpeA.

15              72. An antibody according to claim 71  
wherein said SpeA comprises a change to alanine at  
position 42.

20              73. An antibody according to claim 71  
wherein said SpeA comprises a change to arginine at  
position 42.

25              74. An antibody according to claim 71  
wherein said SpeA comprises a change to alanine at  
position 42 and is fused to an altered SpeB wherein  
said SpeB comprises a change to serine at position 47.

30              75. An antibody according to claim 71  
wherein said SpeA comprises a change to arginine at  
position 42 and is fused to an altered SpeB wherein  
said SpeB comprises a change to serine at position 47.